

REMARKS

Claims 21-22 have been added. No new matter has been introduced by virtue of those new claims. For instance, support for the new claims appears e.g. at page 7, second paragraph of the application.

Claims 7-10, 14, 15 and 20 were rejected under 35 U.S.C. §103(a) over Sasse, et al., The Journal of Antibiotics, 2000, 53, 879-885, in view of Greenwald, Journal of Controlled Release, 2001, 74, 159-171.

As grounds for the rejection, it is stated in the Office Action (page 4) that:

In addition to this, applicant uses the method described in the publication Greenwald, Bioorg. Med. Chem. 1998, 6, 551-562 for the preparation of pegylated molecule of tubulysin. The cited publication of record by the Examiner, Greenwald, Journal of Controlled Release, 2001, 74, 159-171 teaches similar linkers and activation chemistries of the drug molecules.

* * *

Applicants have indicated that the Greenwald reference teaches conjugates of drugs with higher molecule weight PEG (>20,000d). This argument is moot in light of the aforementioned response to arguments. Because, the applicant uses the synthetic methods described in the Greenwald reference to synthesize their tubulysin conjugates.

The rejection is traversed.

As discussed in Applicant's prior response, Greenwald mentions nothing of tubulysin compounds. Thus, Greenwald clearly fails to mention or otherwise suggest any type of PEG conjugates of tubulysin compounds. In the Office Action, it was specifically acknowledged that the primary citation of Sasse et al. does not disclose conjugate compounds of any type.

Moreover, the reference in Applicant's application to Greenwald, Bioorg. Med. Chem. 1998, 6, 551-562 does not somehow that Greenwald, Journal of Controlled Release, 2001, 74, 159-171 is a legitimate citation in the present rejection.

An Applicant's own disclosure can not be relied upon to substantiate a rejection under Section 103.

Moreover, while Applicant fully believe that a *prima facie* case of obviousness does not exist, Applicants submit herewith the Rule 132 Declaration of inventor Alexander Domling, which details data of enhanced results with Applicant's conjugate compounds exhibit enhanced results relative to non-conjugated Tubulysin. See the results at Tables 1 and 2 of the Declaration. See also the results at Table 3 of the Declaration.

In view thereof, reconsideration and withdrawal of the rejection are requested.

Claims 12, 13 and 16-19 stand rejected under 35 U.S.C. 112, first paragraph, although no evidence has been cited to substantiate why the present case might be non-enabling. The rejection is traversed.

The present application fully satisfies the rejection of 35 U.S.C. 112, including the make and use requirements of Section 112, first paragraph.

For instance, tubulysin compounds are disclosed at page 1 of the application. Linkers and polymers are disclosed in detail at page 7. At pages 11 and 12 of the application, specific examples are detailed.

Clearly based on such extensive disclosure as the present application, the skilled worker would have been able to make compounds of the invention.

Therapeutic uses of compounds of are detailed for instance at page 10 of the application. At page 1 of the application, therapeutic activity of tubulysin compounds are disclosed.

Moreover, as discussed in Applicant's prior response, no substantiating reasons have been advanced as to why one skilled in the art could not make and use the claimed invention. Indeed, the discussion above makes clear that one skilled in the art could readily practice the claimed invention in view of Applicants' disclosure.

Respectfully, such a rejection, lacking any supporting evidence or other substantiating grounds is simply not proper. Thus, for example, MPEP §2164.04 states the following (quoting *In re Marzocchi*, 169 USPQ 367):

[I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

Additionally, the enclosed Rule 132 Declaration of Alexander Domling details demonstrated anticancer activity of Applicant's compounds.

In view thereof, reconsideration and withdrawal of the rejection are requested.

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,



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